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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,047	08/04/2003	Roland Maier	01-1385	5291

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
12/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/634,047	MAIER ET AL.	
	Examiner	Art Unit	
	/Mark L. Berch/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7 and 9-20* is/are rejected.

7)☒ Claim(s) *2-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/10/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/10/2008 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5041448.

See example 22, compounds 41 and compound 43, and example 36, compound 139. These are species with 4-piperidinyl-methyl, or 4-piperidinyl-amino, optionally substituted by a methyl, at the 8-position. The claims as presently amended, permits 3-piperidinyl-methyl, or 3-piperidinyl-amino, optionally substituted by a methyl, at the 8-position. Those would be position isomers of the prior art compounds. It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The

isomer is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: ***Ex parte Englehardt***, 208 USPQ 343, 349; ***In re Mehta***, 146 USPQ 284, 287; ***In re Surrey***, 138 USPQ 67; ***Ex Parte Ullyot***, 103 USPQ 185; ***In re Norris***, 84 USPQ 459; ***Ex Parte Naito***, 168 USPQ 437, 439; ***Ex parte Allais***, 152 USPQ 66; ***In re Wilder***, 166 USPQ 545, 548; ***Ex parte Henkel***, 130 USPQ 474; ***Ex parte Biel***, 124 USPQ 109; ***In re Petrzilka***, 165 USPQ 327; ***In re Crownse***, 150 USPQ 554; ***In re Fouche***, 169 USPQ 431; ***Ex parte Ruddy***, 121 USPQ 427; ***In re Wiechert***, 152 USPQ 247, ***In re Shetty***, 195 USPQ 753; ***In re Jones***, 74 USPQ 152, 154; and ***In re Mayne***, 41 USPQ2d 1451 (in which the Court took notice of the extreme similarity between the amino acids Leucine and isoleucine: "In fact, Leu is an isomer of Ile -- an identical chemical formula with differences only in the chemical bonding of the atoms. The side chains...of Leu and Ile have the same number of hydrogen and carbon atoms...The structure of Leu and Ile alone suggest their functional equivalency" (at 1454-1455)).

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (Englehardt) and "Position isomerism is a fact of close structural similarity" (Mehta, emphasis in the original). Note also ***In re Jones***, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to prima facie obviousness"; one of those listed is "adjacent homologues and structural isomers". Position isomers are the basic form of close "structural isomers." Similar is ***In re Schechter and LaForge***, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not

possessed by the prior art compounds." Note also ***In re Deuel*** 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds ... a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (e.g., ortho v. para)." See also MPEP 2144.09, second paragraph.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-12, 14-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for obesity and Type II diabetes, does not reasonably provide enablement for type I diabetes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Pursuant to ***In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples;

and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see ***In re Vaeck***, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims. The claims cover billions of species.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See ***In re Fisher***, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage range information on does not take into account the weight of subject (normally, dosages are given in mg/kg). Moreover, this is generic, the same for the many disorders covered by the specification.

(4) State of the Prior Art: These compounds are xanthines with a particular substitution pattern at the 7- and 8-positions. So far as the examiner is aware, no xanthines of any kind have been used for the treatment of type I diabetes.

(5) Working Examples: There are none for the treatment of any disease. There is a test showing that these compounds are inhibitors of DPP-IV, but this is not a standard test for any of these utilities.

(6) Skill of those in the art: Type I Diabetes treatment, what little there is, tends to be via immune suppressants, since this is an auto-immune disorder. The skill level for the treatment for Type I diabetes is exceptionally low. Type 1 diabetes is an autoimmune disease that results in the irreversible destruction of insulin producing beta cells of the

Langerhans islets in the pancreas. Despite the urgent need --- Type I diabetes is lethal unless the insulin is somehow replaced --- no pharmaceutical has ever been found effective against this disorder. Diet and exercise cannot reverse or prevent type 1 diabetes, although these are important in regulating the insulin given to the patient. Patients are treated either with insulin replacement therapy, or with transplantation surgery, either islet cell transplantation or, less commonly, pancreas transplantation. These do not treat the disorder per se, but only shield the patient from the lethal consequences. Patients may be given drugs for e.g. nephropathy or poor blood circulation in the feet, but these do not treat the disease itself, only the consequences of the lack of insulin.

Further, to rebut this notion that such a DPP-IV inhibitor is suitable for type-1 diabetes, the examiner notes that there is a DPP-IV inhibitor on the market, called Januvia™ (sitaglipin). Specific product information on this drug states explicitly that it is not to be used with patients having Type 1 diabetes. The reference "Patient Information JANUVIA™ " which applicants have provided is presented as an example. This is in fact explicit evidence that not only is treatment of type-1 diabetes with DPP-IV inhibitors not enabled, it is actually contraindicated.

(7) The quantity of experimentation needed: Owing especially to factors 1, 3, 4, 5 and 6, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. ***In re Wright***, 999

F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claims 2-5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark L. Berch/
Primary Examiner
Art Unit 1624

12/2/2008